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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,435	ERLANDER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-20 are pending.

2. This application filed on February 22, 2002, claims benefit of US provisional 60/271,344 filed on February 22, 2001 and US provisional 60/314,697 filed on August 23, 2001.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-20 are indefinite over the recitation of "capable of binding" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited agent have the potential to bind or do in fact bind to the recited ligand. Amendment of the claim to read, for example, "which binds" would obviate this rejection.

B. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim 1 recites detecting a ligand in the preamble of the claim and in the last step of the claim recites detecting said nucleic acid. It is confusing and indefinite because it is not clear whether the ligand and the detectable nucleic acid are one and the same or are whether they are different from each other.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following rejections are based on the broad interpretation of the claims considering that the ligand and detectable nucleic acid are one and the same.

A. Claims 1, 3-8, 13-15, 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Erlander et al. (WO 00/28092).

Erlander et al. teach a method of claim 1, and 19, for detecting a ligand (nucleic acid) in a cell or tissue sample, comprising

(i) contacting said sample with a binding agent (radiolabeled probes), which binds to said ligand (nucleic acid) wherein said agent is attached to a detectable nucleic acid molecule (see page 3, lines 1-2, page 15, lines 19-28);

(ii) staining said sample to identify cells of interest (Nissi-counterstain) (see page 3, line 2);

(iii) capturing or isolating said cells of interest (microdissection of the hybridized cells) (see page 3, lines 13-21);

(iv) and detecting said nucleic acid molecule, wherein the presence of said nucleic acid molecule indicates the presence of said ligand (see page 3, lines 21-26, page 4, lines 11-29).

With regard to claim 3, Erlander et al. teach that said sample is a tissue section (see page 3, lines 1-9);

With regard to claims 4-5, 18, Erlander et al. teach that said detection is done by PCR and quantitative determination of amount of said ligand (see page 4, lines 11-29, page 5, 11-27);

With regard to claim 6, Erlander et al. teach that said staining is by histochemical staining (Nissl-counter stain) (see page 3, line 2);

With regard to claim 7, Erlander et al. teach that said capture is done by laser capture microdissection (see page 3, lines 14-16);

With regard to claims 8 and 20, Erlander et al. teach that said method comprises a plurality of agents (plurality of fluorescently labeled probes, chip or microarray) attached to plurality of different nucleic acids are detected simultaneously to detect plurality of ligands (page 4, lines 12-24, page 5, lines 11-17);

With regard to claims 13-14, Erlander et al. teach that said nucleic acid molecule comprises a T7 promoter (see page 4, lines 12-13, page 12, lines 3-13);

With regard to claim 15, Erlander et al. teach that said detecting comprises contacting the said promoter with T7 polymerase and identifying transcription initiated from said T7 promoter (see page 12, lines 15-27, page 13, lines 1-8).

Thus the disclosure of Erlander et al. meets the limitations in the instant claims.

B. Claims 1-4, 6-12, 19-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Bova (USPN. 6,040,139).

Bova teaches a method of claim 1, and 19, for detecting a ligand (nucleic acid) in a cell or tissue sample, comprising

(i) contacting said sample with a binding agent (antibody), which binds to said ligand (nucleic acid) wherein said agent is attached to a detectable nucleic acid molecule (see column 16, lines 60-67, column 17, lines 1-5, column 12, lines 64-67, column 13, lines 1-35);

(ii) staining said sample to identify cells of interest (counter staining with secondary antibody linked to fluorescent dye) (see column 17, lines 2-10);

(iii) capturing or isolating said cells of interest (microdissection of the fluorescent cells) (see column 17, lines 10-17);

(iv) and detecting said nucleic acid molecule, wherein the presence of said nucleic acid molecule indicates the presence of said ligand (see column 17, lines 18-32).

With regard to claim 2, Bova teaches that said agent is an antibody (see column 16, lines 60-67, column 17, lines 1-5);

With regard to claims 3, 10, 12, Bova teaches that said sample is a tissue section which includes prostrate tissue (see column 17, lines 37-41, column 16, lines 55-59, tissue comprises two cells);

With regard to claims 4, Bova teaches that said detection is done by PCR (see column 17, lines 18-32, column 18, lines 11-46);

With regard to claim 6, Bova teaches that said staining is by histochemical staining (Nissl-counter stain) (see column 16, lines 60-66);

With regard to claim 7, Bova teaches that said capture is done by laser capture microdissection (see column 17, lines 10-17);

With regard to claim 8-9, and 20, Bova teaches that said method comprises a plurality of agents (plurality of antibodies) attached to plurality of different nucleic acids are detected

simultaneously (solid support comprising two cell populations, such as an microarray) to detect plurality of ligands (see column 16, lines 60-67, indicates combination of two antibodies);

With regard to 11, Bova teaches said ligand is prostrate specific ligand (prostrate specific antigen) (see column 13, lines 4-12);

Thus the disclosure of Bova meets the limitations in the instant claims.

C. Claims 1, 3-4, 6, 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gracia et al. (Human Mol. Genet., Vol. 5, No. 5, pages 595-600, 1996).

Gracia et al. teach a method of claim 1, and 19, for detecting a ligand (nucleic acid) in a cell or tissue sample, comprising

(i) contacting said sample (cell line fixed on a slide) with a binding agent (biotinylated cDNA), which binds to said ligand (chromosome containing nucleic acid) (see page 599, column 2, paragraph 2, lines 1-12), wherein said agent is attached to a detectable nucleic acid molecule (see page 599, column 2, paragraph 1, lines 15-17);

(ii) staining said sample to identify cells of interest (Giemsa stained) (see page 599, column 2, paragraph 2, lines 16-17);

(iii) capturing or isolating said cells of interest (microdissection of the hybridized cells) (see page 599, column 2, paragraph 3, lines 1-4);

(iv) and detecting said nucleic acid molecule, wherein the presence of said nucleic acid molecule indicates the presence of said ligand (see page 599, column 2, paragraph 3, lines 9-14, page 600, column 1, paragraph 1-2, page 596, column 1, paragraphs 1-2, Fig.2, wherein the hybridization signal in homogeneously staining regions (hsrs) is indicative of the presence of said ligand (cDNA)).

With regard to claim 3, Gracia et al. teach that said sample is a tissue section (see page 599, column 1, paragraph 1);

With regard to claim 4, Gracia et al. also teach that said detection is done by PCR amplification (see page 599, column 2, paragraph 3, lines 9-14, page 600, column 1, paragraph 1-2);

With regard to claim 6, Gracia et al. teach that said staining is by histochemical staining (see page 599, column 2, paragraph 2, lines 16-17).

Thus the disclosure of Gracia et al. meets the limitations in the instant claims.

D. Claims 1, 2-3, 6, 16-17, 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Englert et al. (Cancer Res, Vol. 60, pages 1526-1530, 2000).

Englert et al. teach a method of claim 1, and 19, for detecting a ligand (nucleic acid, protein) in a cell or tissue sample, comprising

(i) contacting said sample (tumor samples fixed on a slide) with a binding agent (^{33}P-labeled cDNA), which binds to said ligand (nucleic acid) (see page 1527, column 2, paragraph 1-2), wherein said agent is attached to a detectable nucleic acid molecule (see page 1527, column 2, paragraph 1);

(ii) staining said sample to identify cells of interest (-enzyme chemiluminescent label - ECL) (see page 1528, column 1, lines 5-9);

(iii) capturing or isolating said cells of interest (capturing or selectively identifying hybridized cells on gel) (see page page 1527, Fig.1, wherein capturing the hybridization molecules is shown, page 1528, column 1, lines 1-9);

(iv) and detecting said nucleic acid molecule, wherein the presence of said nucleic acid molecule indicates the presence of said ligand (see page 1527, Fig. 1 wherein the hybridization signal in dissected intact cells is indicative of the presence of said ligand (cDNA)).

With regard to claim 2, Englert et al. teach that said agent is antibody (see page 1526, column 2, paragraph 3);

With regard to claim 3, Englert et al. teach that said sample is a tissue section (see page 1527, column 2, paragraph 2);

With regard to claim 10, Englert et al. teach that said sample is prostrate tissue (see page 1527, column 2, paragraph 2);

With regard to claim 11, Englert et al. teach said ligand is prostrate specific ligand (PSA) (see page 1526, column 2, paragraph 3);

With regard to claim 12, Englert et al. teach that said capturing is of one to two cells (tissue cell population contains two or more cells) (see page 1527, Fig. 1, capturing intact cell populations, plurality includes two);

With regard to claims 16-17, Englert et al. teach that said ligand comprises two forms of a polypeptide, phosphorylated (active form) and unphosphorylated (inactive form) (see page 1528, column 1, Fig.2D, showing active form of MMP-2 polypeptide, page 1527, column 1, paragraph 1, indicates that the ligand comprises MMp-2 polypeptide having two forms).

Thus the disclosure of Englert et al. meets the limitations in the instant claims.

E. Claims 1, 3-7, 18-19 are rejected under 35 U.S.C. 102(a) as being anticipated by

Ehrig et al. teach a method of claim 1, and 19, for detecting a ligand (nucleic acid) in a cell or tissue sample, comprising

(i) contacting said sample (tissue sample) with a binding agent (nuclear dyesas toluidine, azure B and methyl green), which binds to said ligand (nucleic acid), wherein said agent is attached to a detectable nucleic acid molecule (see page 23, column 1, paragraph 1, lines 1-11);

(ii) staining said sample to identify cells of interest (bluing solution) (see page 23, column 1, paragraph 1, lines 1-18);

(iii) capturing or isolating said cells of interest (microdissection of the stained cells) (see page 23, column 1, paragraph 2);

(iv) and detecting said nucleic acid molecule, wherein the presence of said nucleic acid molecule indicates the presence of said ligand (see page 23, column 2, paragraph 2);

With regard to claim 3, Ehrig et al. teach that said sample is a tissue section (see page 22, column 2, paragraphs 1-2);

With regard to claims 4-5, Ehrig et al. teach that said detection is done by quantitative PCR amplification (see page 23, column 2, paragraph 2).

With regard to claim 6 Ehrig et al. teach that said staining is by histochemical staining (see page 23, column 1, paragraph 1);

With regard to claim 7, Ehrig et al. teach said capturing is laser capture microdissection (see page 23, column 1, paragraph 2);

With regard to claim 18, Ehrig et al. teach that said quantitative determination includes determination of amount of ligand (nucleic acid captured) (see page 23, column 2, paragraph 2).

Thus the disclosure of Ehrig et al. meets the limitations in the instant claims.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
May 26, 2004

JEHANNE SITTON
PRIMARY EXAMINER
5/27/04